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CARCINOSARCOMA OF GALLBLADDER: A CASE REPORT

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ABSTRACT
Carcinosarcoma of Gall bladder is an uncommon neoplasm, characterized by malignancy of both epithelial and mesenchymal components. Its diagnosis is based on presence and intermingling of these two components. We report a case of 52 year old female patient with complaint of pain and lump in abdomen. CT scan examination showed mass in gall bladder with presence of stones. The patient was treated with cholecystectomy. Histopathological examination of gall bladder mass showed two components consisting of adenocarcinoma and spindle cell sarcoma of gall bladder origin, features consistent with carcinosarcoma. The diagnosis was further confirmed by expression of cytokeratin and vimentin by the respective tumor cells on immunohistochemistry.

INTRODUCTION

Gall Bladder cancers account for 1 to 2% of all cancers, adenocarcinoma being the most common malignant neoplasm among it. In contrast, carcinosarcoma of gall bladder is an extremely atypical subset of malignancy constituting less than 1% [1]. It is a rare malignancy characterized by presence of both malignant epithelial and mesenchymal components. The clinical presentation of these patients is like that of cholecystolithiasis but behavior of this tumor is very aggressive with poor prognosis.

Currently, fewer than 100 cases have been reported in the English literature. Therefore, knowledge and experience regarding this disease is limited [2]. Here we present a case of carcinosarcoma of gall bladder in 52 year old woman.

Case report

A 52 year old female came with complaints of pain in right hypochondrium and weight loss since 3 months. Patient had past history of jaundice one month back. On clinical examination, she had tenderness in the right hypochondriac region. Laboratory investigations showed a white blood cell count of 15,300cells /mm^2, haemoglobin 6.8gm/dl, and platelet count-3.22lakh/cumm. At the time of presentation her Liver Function Tests (LFT's) were normal but her CA 19.9 levels were raised to68.3U/ml. Her chest X-ray showed right CP angle obliteration due to pleural effusion.

USG abdomen showed distended gall bladder with heterogeneous mass and presence of calculi along with mild hepatomegaly. Abdominal CT scan showed diffuse gall bladder distension with intraluminal polypoidal mass. Perforation was noted near fundus of gall bladder. A provisional diagnosis of gall bladder neoplasm with perforation peritonitis was made. Intra-operatively it was thickened and inflamed gall bladder with perforation near fundus. Cholecystectomy was performed. There was pus in sub hepatic space and ascitic fluid in peritoneal cavity. The ascitic fluid and pus culture was positive for Kleibsiella species.

Grossly the cholecystectomy specimen was measuring 11x5x2cm, with congested and thickened serosal surface. A polypoidal mass measuring 6.5x2.5x1.5cm was seen in the body of gall bladder. (Figure1) The mass was solid, grey white in appearance with few haemorrhagic, friable necrotic areas.

Microscopically a biphasic tumour with both carcinomatous and sarcomatous elements was seen. The carcinomatous element was in the form of adenocarcinoma comprising of infiltrating glands lined by epithelium

showing features of malignancy. (Figure2) The sarcomatous elements composed of fascicles of spindle shaped cells which showed nuclear pleomorphism. Both the components were admixed with each other.(Figure3) Immunohisto chemistry demonstrated positivity for cytokeratin in the adenocarcinoma glands (Figure 4) and vimentin was expressed by spindle cells in sarcomatous component.(Figure 5) Heterologous elements were not seen. The tumour was seen infiltrating through the muscularis propria. This patient was treated with cholecystectomy and no adjuvant chemotherapy or radiotherapy was given since the tumour was confined to the gall bladder.

Fig 1. Showing polypoidal growth in gall bladder with few areas of necrosis and congestion

Fig 2. Showing normal gall bladder mucosa transforming into infiltrating adenocarcinoma.[10X]

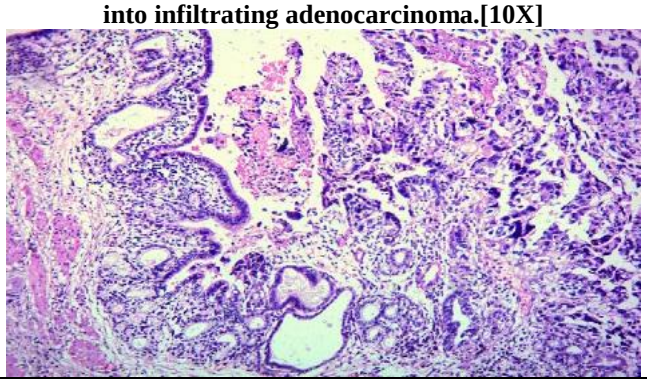


Fig 3. Showing glands with nuclear features of malignancy along with sarcomatous components [40X]

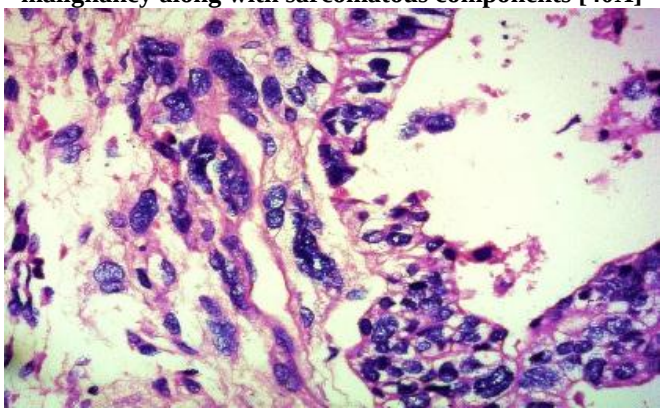


Fig.4 Showing adenocarcinoma component [A, 40X] along with cytokeratin positivity on IHC [B, 10X]

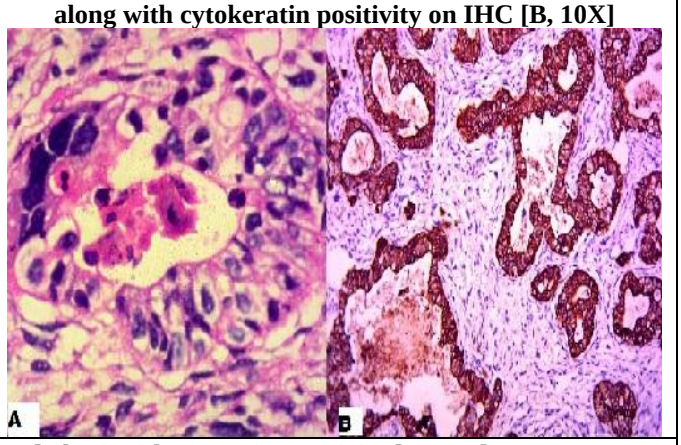
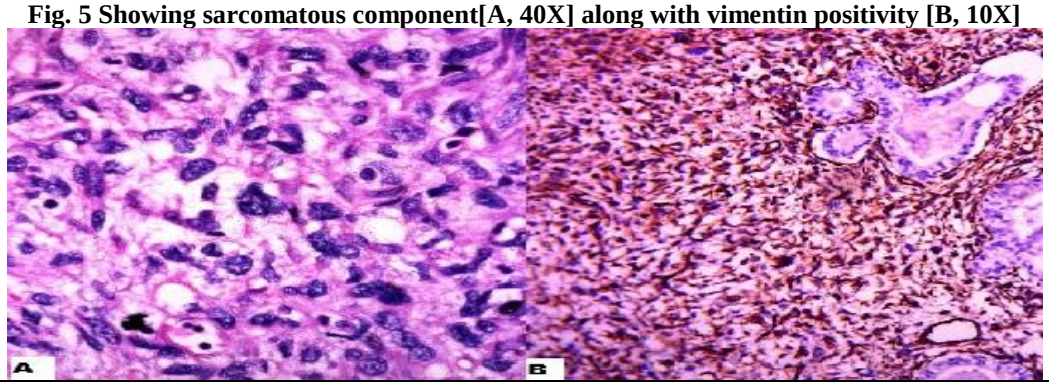


Fig. 5 Showing sarcomatous component[A, 40X] along with vimentin positivity [B, 10X]



DISCUSSION

Carcinosarcoma of gall bladder is an uncommon neoplasm comprises less than 1% of all gall bladder cancers and characterized by the presence of variable proportion of carcinomatous and sarcomatous elements. The term carcinosarcoma was first used as descriptive term by Virchow in 1864. The first case of carcinosarcoma in the gall bladder reported by Landsteiner in 1907 was found in museum specimen [3]. Carcinosarcoma could occur at almost all major organs, such as lung, kidney, upper aerodigestive tract, salivary gland, thyroid, thymus and gastrointestinal tract with its most common site being uterus [4].

Histogenesis of carcinosarcoma is unclear, whether it is due to concurrent transformation of epithelial and mesenchymal cell line in the same organ or that the spindle cell component represents sarcomatous metaplasia in a poorly differentiated carcinoma is debatable [5]. Several theories have been proposed to explain the admixture of the epithelial and the mesenchymal tissues in these neoplasms: (1) a mesenchymal reaction, (2) a true sarcoma, (3) a malignant proliferation of epithelial origin,(4) an embryonic cell rest origin, and (5) the totipotential stem cell hypothesis. The sarcomatous change of a carcinoma can be induced by radiotherapy, alterations to the *p53* gene, and production of the bone morphogenetic protein by cancer cells [6].

The gallbladder carcinosarcoma is more common in females M:F=1:2 to1:5 .The average age range of cancer occurrence is in 60–70 years old individuals. The clinical behavior of this neoplasm is extremely aggressive with median survival time of 5.5 months. However the longest post surgery survival time reported in literature is 60 months [4]. In a cohort study of 26 gallbladder carcinosarcoma cases done by Huguet *et al*., [5], only 3 cases had survival time over 12 months. Currently, fewer than 100 cases of this neoplasm have been reported in the English literature [2].

Patients with gallbladder carcinosarcoma often present with vague abdominal symptoms, such as dull abdominal pain, nausea, weight loss and jaundice. Occasionally, there is a palpable right upper quadrant mass. About 74% of the gallbladder carcinosarcoma cases are associated with cholecystolithiasis and ultrasounds often show a polypoidal mass. An accurate preoperative diagnosis of CSGB is very difficult because imaging studies cannot differentiate it from other malignant neoplasms of the gall bladder. An abdominal angiography often shows neovascularity, whereas Computed Tomography (CT) shows an enhanced solid mass lesion. The differential diagnosis includes gall bladder malignancy, calcified gall stones, or a porcelain gall bladder, when there is calcification seen on CT scan. Carcinosarcoma (CSGB) is not associated with specific radiological findings or serum marker. However the serum levels of tumor marker CA19.9 may be elevated in CSGB [5, 6].

Our patient presented with abdominal mass and weight loss. Also it was associated with cholecystolithiasis and showed elevated Sr. CA 19.9 levels. However there was no evidence of calcification in CT scan.

The diagnosis of CSGB is made on microscopic findings and must be confirmed by immune histochemical staining. Microscopically, the diagnosis of CSGB requires the presence of both malignant epithelial and mesenchymal elements, though these may be intimately admixed or may show characteristics intermediate between the two cell types. These tumors exhibit sarcomatous differentiation towards specific tissue, which are known as heterologous elements and can be recognized as leiomyosarcoma, rhabdomyosarcoma, osteosarcoma and chondrosarcoma [4]. By immunohistochemistry, the carcinomatous component expresses epithelial markers, such as, cytokeratin and epithelial membrane antigen (EMA), and the sarcomatoid component expresses mesenchymal markers like vimentin, desmin and actin. In CSGB, the sarcomatoid component is negative for epithelial markers, such as, cytokeratin, EMA, whereas sarcomatoid carcinoma is positive for epithelial markers, such as, cytokeratin and EMA [1]. Our case showed epithelial positivity for cytokeratin and sarcomatous component was highlighted by vimentin. However no heterologous elements were seen in present case.

Therapeutic interventions have not been well defined and no optimal postoperative adjuvant therapy, such as, chemotherapy and radiation therapy, has been established because of the rarity of CSGB and its poor prognosis. CSGB is treated in the same way as other gallbladder cancers. Accordingly, the best treatment option is surgical excision. Cholecystectomy alone is sufficient for cancer cells confined to the lamina propria, whereas more advanced states require resection of a 3 to 5 cm wedge of liver tissue at the gallbladder bed, combined with LN dissection in the absence of evidence of distant metastasis [1].

To conclude, extensive sampling for histopathological examination and careful search for various carcinomatous and sarcomatous elements on microscopy are mandatory for making accurate diagnosis of carcinosarcoma of gall bladder.

CONCLUSION

Carcinosarcoma of gall bladder is rare entity, characterized by presence of both malignant epithelial and mesenchymal components with a poorer prognosis than gall bladder adenocarcinoma. More clinicopathological data and further studies are required to identify the prognostic indicators and histogenesis of gall bladder carcinosarcoma.

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